AMENDMENTS

Please cancel claims 1 and 2, without prejudice or disclaimer. Please amend claims 5 and 7 and add new claim 9.

1. (cancelled)

2. (cancelled)

3. (original) An isolated nucleic acid molecule comprising the nucleic acid sequence presented in SEQ ID NO: 1.

4. (original) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

5. (currently amended) A recombinant expression vector comprising the ~~isolated~~ nucleic acid molecule of claim [1] 3.

6. (previously presented) A host cell comprising the recombinant expression vector of claim 5.

7. (currently amended) A recombinant expression vector comprising the ~~isolated~~ nucleic acid molecule of claim 4.

8. (previously presented) A host cell comprising the recombinant expression vector of claim 7.

9. (new) An isolated nucleic acid molecule comprising a sequence that:

(a) encodes the amino acid sequence of SEQ ID NO: 2; and

(b) hybridizes under stringent conditions with wash conditions of 0.1xSSC/0.1% SDS at 68°C to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof.

RESPONSE

I. Status of the Claims

Claims 1 and 2 have been cancelled without prejudice or disclaimer. Claims 5 and 7 have been amended and new Claim 9 has been added. Claims 3-9 are therefore presently pending in the case.

II. Support for the Amended Claims

Claim 5 has been amended to further clarify the claim and to depend on Claim 3 rather than cancelled Claim 1. Amendment of Claim 5 finds support in original Claim 5 and throughout the specification as originally filed, with particular support being found at least on page 17, line 10-15. In addition claim s 5 and 7 have been amended to remove the term isolated which was inappropriate in the context of the claim.

New Claim 9 has been added to better claim the present invention. New Claim 9 finds support in original Claim 2 and throughout the specification as originally filed.

Amendments to claim 5 and 7 and new claim 9 are fully supported by the specification and claims as originally filed, they do not constitute new matter. Entry, therefore, is respectfully requested

III. Rejection of Claims Under 35 U.S.C. § 101

The Advisory Action maintains the pending rejection of claims 1-8 under 35 U.S.C. § 101, allegedly because the claimed invention lacks support by either a specific and substantial asserted utility or a well established utility. Applicants respectfully continue to traverse.

Previous Office Actions and the Advisory Action clearly indicate that the Examiner does not believe that the sequences of the present invention have patentable utility. Applicants strongly disagree and for the sake of clarity and in order to have presented the case and claims in the most complete condition prior to allowance or appeal, reiterate some of those utilities. Applicants submit that the specification details a number of specific and substantial utilities for the presently claimed polynucleotide sequences, including the detection and diagnosis of human diseases such as *inter alia*, diabetes, abnormal body weight or obesity, atherosclerosis, mental disorders, disorders of the immune system, heart disease, abnormal blood pressure, cancer, and

any associated symptoms (specification at page 7, lines 14-17). Additional uses include assessing temporal and tissue specific gene expression patterns (specification at page 9, line 25), particularly using a high throughput "chip" format (specification at page 8, line 33 through page 9, line 22), mapping the sequences to a specific region of a human chromosome and identifying protein encoding regions (specification at page 14, line 1-9), determining the genomic structure (specification at page 14, line 1-9), and in diagnostic assays such as forensic analysis, human population biology and paternity determinations (see, for example, the specification from page 14, line 1-9).

Applicants note that the fact that a sequence sharing100% identity at the amino acid level with the sequences of the present invention is present in the leading scientific repository for protein sequence data (SwissProt), and has been annotated by third party scientists *wholly unaffiliated with Applicants* as human olfactory receptor 2B6 (Hs6M1-32) (Olfactory receptor 6-31) (SwissProt Accession No. P58173; alignment and report provided in **Exhibit A**). The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this SwissProt annotation, there can be little question that those skilled in the art would clearly believe that Applicants' sequence is a novel human G protein-coupled receptor, as set forth in the specification as originally filed. Thus, clearly, as this protein was annotated by those of skill in the art in no way associated with Applicants. Thus clearly , Applicants' assertion regarding the function and utility of the protein of the present invention is credible and the present claims meet the requirements of 35 U.S.C. § 101.

The Advisory Action takes the position that neither the specification nor the art of record disclose any diseases or conditions associated with the function or expression of the protein encoded by the sequences of the present invention. Applicants disagree, as the specification discloses a number of diseases or conditions associated with the function or expression of the protein encoded by the sequences of the present invention as well as several specific and substantial utilities for the presently claimed polynucleotide sequences, which encode a the human G protein-coupled receptor, olfactory receptor 2B6. These utilities include detection, diagnosis and development of therapeutics directed at, *inter alia*, abnormal body weight or obesity, atherosclerosis and heart disease. These disorders can all be affected by an individual's sense of taste and smell, senses that those of skill in the art would recognize as related to

olfactory receptor function and activity.

Furthermore, it is well known to the art that novel human G-protein coupled receptors have a well-established utility. This assertion is evidenced by the fact that 60% of these drugs target G-protein coupled receptors as described in the previously submitted publication by Gurrath, 2001 (Curr. Med. Chem. *8*:1605-1648). In addition, Applicants' assertion, that the presently described sequences have specific, credible and well-established utility, is also supported by the fact that multiple millions of dollars are allocated yearly in the identification and targeting of G-protein coupled receptors such as those of present invention. If these molecules did not have well-established utility recognized by those of skill in the art in the pharmaceutical industry, surely those in such a competitive industry would not direct so much of their limited resources towards this class of receptors.

Additionally, methods similar to those of the present invention were used to identify the G protein-coupled receptor of issued U.S. Patent 6,043,052. Issued U.S. Patents are presumed to be valid and to meet the requirements of 35 U.S.C. §§ 101, 102, 103 and 112, specifically, that they have utility, are novel, non-obvious, are enabled, meet the written description requirements and particularly point out and distinctly claim the invention. Therefore, the Applicants' assertion that the described G protein-coupled receptor is in fact a G protein-coupled receptor is supported by issued U.S. Patent 6,043,052, as well as the plethora of other G protein-coupled receptor patents that the office has issued. For example, the specific and substantial utility of human G protein-coupled receptors is evidenced by the fact that they are the subject of the above mentioned U.S. Patent No. 6,043,052 which discloses polynucleotides encoding a novel GPCR and U.S. Patent Nos. 5,891,646 and 6,110,693, both of which disclose and claim methods for detecting G protein-coupled receptor activity *in vivo* and *in vitro*, methods for assaying GPCR activity, and methods of screening for G protein-coupled receptor ligands, G protein-coupled receptor kinase activity, components that interact with G protein-coupled receptors regulatory processes and constructs useful in such methods. The issuance of these U.S. patents clearly indicates that GPCR polynucleotides have utility and that such utilities were sufficiently specific and substantial to warrant the issuance of U.S. patents directed to methods used to identify and characterize G protein-coupled receptors. The teachings of these patentable disclosures are directly applicable to the present invention (G protein-coupled receptor polynucleotides) and are evidence that those skilled in the art recognize the specific and substantial utility of G protein-

coupled receptors. In light of the issuance of U.S. Patent No. 6,043,052 on polynucleotides encoding a novel G protein-coupled receptor, Applicants respectfully submit that the present application, which also describes polynucleotides encoding a novel G protein-coupled receptor, specifically olfactory receptor 2B6, describes an invention with specific and substantial utility fully compliant with 35 U.S.C. § 101.

Thus, the skilled artisan would readily appreciate the utilities asserted by Appllicants' regarding the role of the proteins encoded by sequences of the present invention in abnormal body weight or obesity, atherosclerosis and heart disease associated with the provision of a human G protein-coupled receptor, olfactory receptor 2B6. Therefore, the present utility rejection must fail. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

Clearly evidence supports Applicants' assertions that the sequences of the present invention which encode a human G protein-coupled receptor, olfactory receptor 2B6, which have utility that is recognized by those of skill in the art. Furthermore, this situation is similar to Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence (such as the presently claimed sequence) that has a similarity to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase . Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA. .....Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed..... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made."

The present case is similar to that presented in Example 10 of the Revised Interim Utility

Guidelines Training Materials in that the sequences of the present invention are identical to those that are recognized by those of skill in the art, in no way affiliated with Applicants, to encode a human G-protein coupled receptor, specifically human olfactory receptor 2B6. Thus the rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should be overruled.

The Final Office Action and the Advisory Action also discount Appllicants' assertion regarding the use of the presently claimed polynucleotides on DNA gene chips, based on the position that such a use would allegedly be generic. Further, these Actions seem to be requiring Appllicants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet the requirements of § 101. Applicants respectfully point out that knowledge of the exact function or role of the presently claimed sequence is not required to track expression patterns using a DNA chip. As set forth in at least Applicants Response to Final, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details at least at page 8, line 33 through page 9, line 22. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, as well as more recently issued U.S. Patent Nos. 5,837,832, 6,156,501 and 6,261,776.

The Board is further requested to consider that, given the huge expense of the drug discovery process, even negative information has great "real world" practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in general, in that time and resources are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly, compositions that enhance the utility of such DNA gene chips, such as the presently claimed sequences encoding human olfactory receptor 2B6, must in themselves be useful. Moreover, the presently described human olfactory receptor provides uniquely specific sequence resources for identifying and

quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression.

Additionally, only a small percentage of the genome (2-4%) actually encodes exons, which in turn encode amino acid sequences. Thus, not all human genomic DNA sequences are useful in such gene chip applications. This further discounts the Examiner's position that such uses are "generic". The present claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co., for substantial sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

Given the physiologic activity and importance of G protein-coupled receptors known to those of skill in the art, those of skill in the art would readily appreciate the importance of tracking the expression of the genes encoding the described proteins, particularly due to well established role of G protein-coupled receptors in the pharmaceutical industry. In the present case this apparent utility is further bolstered by the expression of the sequences of the present invention in the prostate, a tissue which when involved in cancer often under goes multiple drug resistance. The use of the claimed polypeptide in an array for screening purposes Appllicants respectfully point out that nucleic acid sequences have the greatest specific utility in gene chip applications once the role of the sequence has been identified, as have tissues of interest, as in the present case. Once the role of the particular nucleic acid is known, the level of gene expression has and even greater significance. By identifying the physiological activity role of the claimed sequence, the claimed sequence has a far greater utility in gene chip applications that just any random piece of DNA. Appllicants respectfully submit that **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, is distinct from the requirement for a **unique** utility, which is clearly an improper standard. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Therefore, just because other nucleic acid sequences find utility in gene chip applications does not mean that the use of Appllicants' sequence in gene chip applications is not a specific utility. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile tires have the exact same utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility - specifically, use in the

game of golf. All cancer treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the specific utility the present nucleotide sequence has in determining the genomic structure of the corresponding human chromosome (specification at page 14, lines 1-9) , for example mapping the protein encoding regions as described in the specification (specification at page 14, lines 1-9) and evidenced below. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequence. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Only a minor percentage of the genome actually encodes exons, which in turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.,* showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* defines that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The

Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence supporting the Applicants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

As still further evidence supporting Appllicants' assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions has been provided in a previous exhibit. This exhibit was the result of a blast analysis using SEQ ID NO:1 of the present invention when compared to the identified human genomic sequence and provides evidence of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome on which this protein is encoded as chromosome 6 and that this gene was contained within BAC clone AL133267. Thus clearly one would not have been able to identify the chromosome which encodes the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were.

Thus, the question of utility is a straightforward one. As set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S.

Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

In *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and

development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (C.C.P.A. 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Finally, with regards to the issue of due process, while Applicants are well aware of the new Utility Guidelines set forth by the USPTO, Applicants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Applicants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants agree that each application is examined on its own merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these

patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Given the rapid pace of development in the biotechnology arts, it is difficult for the Applicants to understand how an invention fully disclosed and free of prior art at the time the present application was filed, could somehow retain *less* utility and be *less* enabled than inventions in the cited issued U.S. patents (which were filed during a time when the level of skill in the art was clearly lower). Simply put, Applicants invention is *more* enabled and retains *at least as much* utility as the inventions described in the claims of the U.S. patents of record. Thus, holding Applicants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

Therefore, those of skill in the art would clearly recognize the utility of the present invention as well as be enabled to make and use the present invention without undue experimentation. Thus, the present invention clearly has credible and well established utility. In light of the evidence presented above and in previous responses, Applicants respectfully submit that the present invention is in full compliance with the provisions of 35 U.S.C. § 101, and respectfully request that the rejection be withdrawn.

IV. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

The Action rejects claims 1-8 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the claimed invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as the pending claims have been shown to have a specific, substantial, credible and well established utility (see above) and that given the clear identification of the present invention as human olfactory receptor 2B6, those of skill in the art would clearly know how to make and use the present invention without undue experimentation. Applicants therefore respectfully request that the rejection of the pending claims under 35 U.S.C. § 112, first paragraph, be withdrawn.

V. Rejection of Claims 1-2 and 5-6 Under 35 U.S.C. § 112, First Paragraph

The Advisory Action rejects Claim 1-2 and 5-6 due allegedly to a lack of enablement and written description. While Applicants in no way agree with the rejection, as claims 1 and 2 have been cancelled without prejudice or disclaimer this rejection has been avoided. Claim 5 has been amended such that it is no longer dependent on cancelled Claim 1 and thus the rejection of Claim 5 and its dependent Claim 6 under 35 U.S.C. § 112, first paragraph has also been avoided. Applicants therefore respectfully request withdrawal of this pending rejection.

VI. Conclusion

The present document is a full and complete response to the pending issues in this case. In conclusion, Applicants submit that, in light of the foregoing amendments and remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Brunner have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

September 29, 2003
Date

Peter G Sebarnan Reg No 40162

Lance K Ishimoto Reg. No. 41,866

LEXICON GENETICS INCORPORATED
8800 Technology Forest Place
The Woodlands, TX 77381
(281) 863-3333

Customer # 24231

NiceProt View of Swiss-Prot: P58173

Entry information

Entry name	**O2B6_HUMAN**
Primary accession number	**P58173**
Secondary accession number	Q9H5B0
Entered in Swiss-Prot in	Release 40, October 2001
Sequence was last modified in	Release 40, October 2001
Annotations were last modified in	Release 41, February 2003

Name and origin of the protein

Protein name	**Olfactory receptor 2B6**
Synonyms	**Hs6M1-32** **Olfactory receptor 6-31** **OR6-31**
Gene name	**OR2B6**
From	Homo sapiens (Human) [TaxID: 9606]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

References

[1] SEQUENCE FROM NUCLEIC ACID.
Williams S.;
Submitted (OCT-2000) to the EMBL/GenBank/DDBJ databases.

Comments

- ***FUNCTION***: Putative odorant receptor.
- ***SUBCELLULAR LOCATION***: Integral membrane protein.
- ***SIMILARITY***: Belongs to family 1 of G-protein coupled receptors.

Copyright

Cross-references

EMBL	AL133267; CAC14158.1; -.
Genew	HGNC:8241; OR2B6.
CleanEx	HGNC:8241; OR2B6.
InterPro	IPR000276; GPCR_Rhodpsn.
Pfam	PF00001; 7tm_1; 1.
PRINTS	PR00237; GPCRRHODOPSN.

PROSITE	PS00237; G_PROTEIN_RECEP_F1_1; 1. PS50262; G_PROTEIN_RECEP_F1_2; 1.
Implicit links to	Ensembl; ProDom; HOVERGEN; BLOCKS; ProtoNet; ProtoMap; PRESAGE; DIP; ModBase; SWISS-2DPAGE.

Keywords

G-protein coupled receptor; Transmembrane; Glycoprotein; Multigene family; Olfaction.

Features

Key	From	To	Length	Description
DOMAIN	1	25	25	EXTRACELLULAR (*POTENTIAL*).
TRANSMEM	26	49	24	1 (*POTENTIAL*).
DOMAIN	50	57	8	CYTOPLASMIC (*POTENTIAL*).
TRANSMEM	58	79	22	2 (*POTENTIAL*).
DOMAIN	80	100	21	EXTRACELLULAR (*POTENTIAL*).
TRANSMEM	101	120	20	3 (*POTENTIAL*).
DOMAIN	121	139	19	CYTOPLASMIC (*POTENTIAL*).
TRANSMEM	140	158	19	4 (*POTENTIAL*).
DOMAIN	159	195	37	EXTRACELLULAR (*POTENTIAL*).
TRANSMEM	196	219	24	5 (*POTENTIAL*).
DOMAIN	220	236	17	CYTOPLASMIC (*POTENTIAL*).
TRANSMEM	237	259	23	6 (*POTENTIAL*).
DOMAIN	260	272	13	EXTRACELLULAR (*POTENTIAL*).
TRANSMEM	273	292	20	7 (*POTENTIAL*).
DOMAIN	293	313	21	CYTOPLASMIC (*POTENTIAL*).
DISULFID	97	189		*BY SIMILARITY*.
CARBOHYD	5	5		N-LINKED (GLCNAC...) (*POTENTIAL*).

Sequence information

Length: **313 AA**
Molecular weight: **35414 Da**
CRC64: **71D459541ACF5301** [This is a checksum on the sequence]

```
          10         20         30         40         50         60
           |          |          |          |          |          |
MNWVNDSIIQ EFILLGFSDR PWLEFPLLVV FLISYTVTIF GNLTIILVSR LDTKLHTPMY

          70         80         90        100        110        120
           |          |          |          |          |          |
FFLTNLSLLD LCYTTCTVPQ MLVNLCSIRK VISYRGCVAQ LFIFLALGAT EYLLLAVMSF

         130        140        150        160        170        180
           |          |          |          |          |          |
DRFVAICRPL HYSVIMHQRL CLQLAAASWV TGFSNSVWLS TLTLQLPLCD PYVIDHFLCE

         190        200        210        220        230        240
           |          |          |          |          |          |
VPALLKLSCV ETTANEAELF LVSELFHLIP LTLILISYAF IVRAVLRIQS AEGRQKAFGT
```

```
        250         260         270         280         290         300
          |           |           |           |           |           |
CGSHLIVVSL FYSTAVSVYL QPPSPSSKDQ GKMVSLFYGI IAPMLNPLIY TLRNKEVKEG

        310
          |
FKRLVARVFL IKK
```

>P58173 ACCESSION:P58173 NID: Homo sapiens (Human). Olfactory receptor 2B6 (Hs6M1-32) (Olfactory receptor 6-31) (OR6-31).
sp_tr_nrdb
Length = 313

Score = 621 bits (1601), Expect = e-177
Identities = 313/313 (100%), Positives = 313/313 (100%)

```
Query: 1   MNWVNDSIIQEFILLGFSDRPWLEFPLLVVFLISYTVTIFGNLTIILVSRLDTKLHTPMY 60
           MNWVNDSIIQEFILLGFSDRPWLEFPLLVVFLISYTVTIFGNLTIILVSRLDTKLHTPMY
Sbjct: 1   MNWVNDSIIQEFILLGFSDRPWLEFPLLVVFLISYTVTIFGNLTIILVSRLDTKLHTPMY 60

Query: 61  FFLTNLSLLDLCYTTCTVPQMLVNLCSIRKVISYRGCVAQLFIFLALGATEYLLLAVMSF 120
           FFLTNLSLLDLCYTTCTVPQMLVNLCSIRKVISYRGCVAQLFIFLALGATEYLLLAVMSF
Sbjct: 61  FFLTNLSLLDLCYTTCTVPQMLVNLCSIRKVISYRGCVAQLFIFLALGATEYLLLAVMSF 120

Query: 121 DRFVAICRPLHYSVIMHQRLCLQLAAASWVTGFSNSVWLSTLTLQLPLCDPYVIDHFLCE 180
           DRFVAICRPLHYSVIMHQRLCLQLAAASWVTGFSNSVWLSTLTLQLPLCDPYVIDHFLCE
Sbjct: 121 DRFVAICRPLHYSVIMHQRLCLQLAAASWVTGFSNSVWLSTLTLQLPLCDPYVIDHFLCE 180

Query: 181 VPALLKLSCVETTANEAELFLVSELFHLIPLTLILISYAFIVRAVLRIQSAEGRQKAFGT 240
           VPALLKLSCVETTANEAELFLVSELFHLIPLTLILISYAFIVRAVLRIQSAEGRQKAFGT
Sbjct: 181 VPALLKLSCVETTANEAELFLVSELFHLIPLTLILISYAFIVRAVLRIQSAEGRQKAFGT 240

Query: 241 CGSHLIVVSLFYSTAVSVYLQPPSPSSKDQGKMVSLFYGIIAPMLNPLIYTLRNKEVKEG 300
           CGSHLIVVSLFYSTAVSVYLQPPSPSSKDQGKMVSLFYGIIAPMLNPLIYTLRNKEVKEG
Sbjct: 241 CGSHLIVVSLFYSTAVSVYLQPPSPSSKDQGKMVSLFYGIIAPMLNPLIYTLRNKEVKEG 300

Query: 301 FKRLVARVFLIKK 313
           FKRLVARVFLIKK
Sbjct: 301 FKRLVARVFLIKK 313
```